

FIG._ 1A

SEQ ID NO: 1

Nucleotide Sequence Tankyrase Homologue isotype1

CTTTGAAGACACTGGATTTTCATACTTTTGCCTGGGGTTATCTCTCTGTGTCTCACTACATAGACAAATA
TTAGCTGTGAGCAGATCTTTTTTTGTTGCTTCTTGTAGTCCCCCAGTTTAGCAGAAACATTCTGTGAGA
TAGATGTGGGAAAGGAATTCTAGCAAGAGTTTTGTCACTGTATCATAAGGTTGTGATTTACATATTTAA
GTTTTATACTTTGAACATCTGAAAATGTATACATACTAAATATGCAGAACTCTATTGTAGAGTGAGAAA
CATTTGAACTTTGAGCTTTTCACTCACTTATTTTGTATTCTTTCTTTGAGGTTAGCAGTAGTACCACCCA
AGGCACTGCTTAGGTACCACTGCTGCTTAGTGGAGAGTCCCTCTGGCTTTATCATTAAAGGTTTTGGGCG
GAAAGACGTAGTTGAATATTTGCTTCAGAATGGTGCAAGTGTCCAAGCACGTGATGATGGGGGCCTTAT
TCCTCTTCATAATGCATGCTCTTTTGGTCATGCTGAAGTAGTCAATCTCCTTTTGGCAGATGGTGCAGA
CCCCAATGCTCGAGATAATTGGAATTATACTCCTCTCCATGAAGCTGCAATTAAAGGAAAGATTGATGT
TTGCATTGTGCTGTTACAGCATGGAGCTGAGCCAACCATCCGAAATACAGATGGAAGGACAGCATTGGA
TTTAGCAGATCCATCTGCCAAAGCAGTGCTTACTGGTGAATATAAGAAAGATGAACTCTTAGAAAGTGC
CAGGAGTGGCAATGAAGAAAAAATGATGGCTCTACTCACACCATTAAATGTCAACTGCCACGCAAGTGA
TGGCAGAAAGTCAACTCCATTACATTTGGCAGCAGGATATAACAGAGTAAAGATTGTACAGCTGTTACT
GCAACATGGAGCTGATGTCCATGCTAAAGATAAAGGTGATCTGGTACCATTACACAATGCCTGTTCTTA
TGGTCATTATGAAGTAACTGAACTTTTTGGTCAAGCATGGTGCCTGTGTAAATGCAATGGACTTGTGGCA
ATTCACCTCCTCTTCATGAGGCAGCTTCTAAGAACAGGGTTGAAGTATGTTCTCTTCTCTTAAGTTATGG
TGCAGACCCAACACTGCTCAATTGTCACAATAAAAGTGCTATAGACTTGGCTCCCACACCACAGTTAAA
AGAAAGATTAGCATATGAATTTAAAGGCCACTCGTTGCTGCAAGCTGCACGAGAAGCTGATGTTACTCG
AATCAAAAAACATCTCTCTCTGGAAATGGTGAATTTCAAGCATCCTCAAACACATGAAACAGCATTGCA
TTGTGCTGCTGCATCTCCATATCCCAAAGAAAGCAAATATGTGAACTGTTGCTAAGAAAAGGAGCAAA
CATCAATGAAAAGACTAAAGAATTCTTGACTCCTCTGCACGTGGCATCTGAGAAAGCTCATAATGATGT
TGTTGAAGTAGTGGTGAAACATGAAGCAAAGGTTAATGCTCTGGATAATCTTGGTCAGACTTCTCTACA

CAGAGCTGCATATTGTGGTCATCTACAAACCTGCCGCTACTCCTGAGCTATGGGTGTGATCCTAACAT
TATATCCCTTCAGGGCTTTACTGCTTTACAGATGGGAAATGAAAATGTACAGCAACTCCTCCAAGAGGG
TATCTCATTAGGTAATTCAGAGGCAGACAGACAATTGCTGGAAGCTGCAAAGGCTGGAGATGTCGAAAC
TGTAaaaaaaactGTGTACTGTTcagAGTGTCAACTGCAGAGACATTGAAGGGCGTCAGTCTACACCACT
TCATTTTGCAGCTGGGTATAACAGAGTGTCCGTGGTGAATATCTGCTACAGCATGGAGCTGATGTGCA
TGCTAAAGATAAAGGAGGCCTTGTACCTTGCACAATGCATGTTCTTATGGACATTATGAAGTTGCAGA
ACTTCTTGTTAAACATGGAGCAGTAGTTAATGTAGCTGATTTATGGAAATTTACACCTTTACATGAAGC
AGCAGCAAAAGGAAAATATGAAATTTGCAAACCTTCTGCTCCAGCATGGTGCAGACCCTACCAAAAAA
CAGGGATGGAAATACTCCTTTGGATCTTGTTAAAGATGGAGATACAGATATTCAAGATCTGCTTAGGGG
AGATGCAGCTTTGCTAGATGCTGCCAAGAAGGGTTGTTTAGCCAGAGTGAAGAAGTTGTCTTCTCCTGA
TAATGTAAATTGCCGCGATACCCAAGGCAGACATTCAACACCTTTACATTTAGCAGCTGGTTATAATAA
TTTAGAAGTTGCAGAGTATTTGTTACAACACGGAGCTGATGTGAATGCCAAGACAAAGGAGGACTTAT
TCCTTTACATAATGCAGCATCTTACGGGCATGTAGATGTAGCAGCTCTACTAATAAAGTATAATGCATG
TGTCATGCCACGGACAAATGGGCTTTCACACCTTTCACGGAAGCAGCCCAAAAGGGACGAACACAGCT
TTGTGCTTTGTTGCTAGCCCATGGAGCTGACCCGACTCTTAAAAATCAGGAAGGACAAACACCTTTAGA
TTTAGTTTCAGCGGATGATGTCAGCGCTCTTCTGACAGCAGCCATGCCCCATCTGCTCTGCCCTCTTG
TTACAAGCCTCAAGTGCTCAATGGTGTGAGAAGCCAGGAGCCACTGCAGATGCTCTCTCTTCAGGTCC
ATCTAGCCCATCAAGCCTTTCTGCAGCCAGCAGTCTTGACAACCTTATCTGGGAGTTTTTCAGAACTGTC
TTCAGTAGTTAGTTCAAGTGGAACAGAGGGTGCTTCCAGTTTGGAGAAAAGGAGGTTCCAGGAGTAGA
TTTTAGCATAACTCAATTCGTAAGGAATCTTGGACTTGAGCACCTAATGGATATATTTGAGAGAGAACA
GATCACTTTGGATGTATTAGTTGAGATGGGGCACAAGGAGCTGAAGGAGATTGGAATCAATGCTTATGG
ACATAGGCACAACTAATTAAGGAGTCGAGAGACTTATCTCCGGACAACAAGGTCTTAACCCATATTT
AACTTTGAACACCTCTGGTAGTGGAACAATTCTTATAGATCTGTCTCCTGATGATAAAGAGTTTCAGTC
TGTGGAGGAAGAGATGCAAAGTACAGTTCGAGAGCACAGAGATGGAGGTCATGCAGGTGGAATCTTCAA
CAGATACAATATTCTCAAGATTGAGAAGGTTTGTAAACAAGAACTATGGGAAAGATACACTCACCGGAG
AAAAGAAGTTTCTGAAGAAAACCACAACCATGCCAATGAACGAATGCTATTTTCATGGGTCTCCTTTTGT
GAATGCAATTATCCACAAAGGCTTTGATGAAAGGCATGCGTACATAGGTGGTATGTTTGGAGCTGGCAT
TTATTTTGCTGAAAACCTTCCAAAAGCAATCAATATGTATATGGAATTGGAGGAGGTACTGGGTGTCC
AGTTCACAAAGACAGATCTTGTTACATTTGCCACAGGCAGCTGCTCTTTTGCCGGGTAAACCTTGGGAAA
GTCTTTCCTGCAGTTCAGTGCAATGAAAATGGCACATTCTCCTCCAGGTCATCACTCAGTCACTGGTAG
GCCCAGTGTAATGGCCTAGCATTAGCTGAATATGTTATTTACAGAGGAGAACAGGCTTATCCTGAGTA
TTTAATTACTTACCAGATTATGAGGCCTGAAGGTATGGTCGATGGATAAATAGTTATTTTAAGAACTA
ATTCCACTGAACCTAAAATCATCAAAGCAGCAGTGGCCTCTACGTTTTACTCCTTTGCTGAAAAAAA
AA

FIG. 1B

FIG._2A

SEQ ID NO: 2

Nucleotide Sequence Tankyrase Homologue isotype2

CGCGCTGCTCCGCCCCGCCGCGGGGCAGCCGGGGGGCAGGGAGCCCAGCGAGGGGCGCGCGTGGGCGCGG
CCCATGGGACTGCGCCGGATCCGGTGACAGCAGGGAGCCAAGCGGCCCGGGCCCTGAGCGCGTCTTCTC
CGGGGGGCGCTCGCCCTCCTGCTCGCGGGGCCGGGGCTCCTGCTCCGGTTGCTGGCGCTGTTGCTGGCTG
TGGCGGCGGGCCAGGATCATGTGCGGTCGCCGCTGCGCCGGCGGGGGAGCGGCCTGCGCGAGCGCCGCGG
CCGAGGCCGTGGAGCCGGCCGCCGAGAGCTGTTTCGAGGCGTGCCGCAACGGGGACGTGGAACGAGTCA
AGAGGCTGGTGACGCCTGAGAAGGTGAACAGCCGCGACACGGCGGGCAGGAAATCCACCCCGCTGCACT
TCGCCGCAGGTTTTGGGCGGAAAGACGTAGTTGAATATTTGCTTCAGAATGGTGCAAATGTCCAAGCAC
GTGATGATGGGGGCCTTATTCCTCTTCATAATGCATGCTCTTTTGGTCATGCTGAAGTAGTCAATCTCC
TTTTGCGACATGGTGCAGACCCCAATGCTCGAGATAATTGGAATTATACTCCTCTCCATGAAGCTGCAA
TTAAAGGAAAGATTGATGTTTGCATTGTGCTGTTACAGCATGGAGCTGAGCCAACCATCCGAAATACAG
ATGGAAGGACAGCATTGGATTTAGCAGATCCATCTGCCAAAGCAGTGCTTACTGGTGAATATAAGAAAG
ATGAACTCTTAGAAAGTGCCAGGAGTGGAATGAAGAAAAAATGATGGCTCTACTCACACCATTAAATG
TCAACTGCCACGCAAGTGATGGCAGAAAGTCAACTCCATTACATTTGGCAGCAGGATATAACAGAGTAA
AGATTGTACAGCTGTTACTGCAACATGGAGCTGATGTCCATGCTAAAGATAAAGGTGATCTGGTACCAT
TACACAATGCCTGTTCTTATGGTCATTATGAAGTAACTGAACTTTTGGTCAAGCATGGTGCCTGTGTAA
ATGCAATGGACTTGTGGCAATTCCTCCTCTTCATGAGGCAGCTTCTAAGAACAGGGTTGAAGTATGTT
CTCTTCTCTTAAGTTATGGTGCAGACCCAACACTGCTCAATTGTACAATAAAAGTGCTATAGACTTGG
CTCCACACCACAGTTAAAGAAAGATTAGCATATGAATTTAAAGGCCACTCGTTGCTGCAAGCTGCAC
GAGAAGCTGATGTTACTCGAATCAAAAAACATCTCTCTTGGAATGGTGAATTTCAAGCATCCTCAAA
CACATGAAACAGCATTGCATTGTGCTGCTGCATCTCCATATCCCAAAGAAAGCAAATATGTGAACTGT
TGCTAAGAAAAGGAGCAAACATCAATGAAAAGACTAAAGAATTCTTGACTCCTCTGCACGTGGCATCTG
AGAAAGCTCATAATGATGTTGTTGAAGTAGTGGTGAAACATGAAGCAAAGGTTAATGCTCTGGATAATC

TTGGTCAGACTTCTCTACACAGAGCTGCATATTGTGGTCATCTACAAACCTGCCGCCTACTCCTGAGCT
ATGGGTGTGATCCTAACATTATATCCCTTCAGGGCTTTACTGCTTTACAGATGGGAAATGAAAATGTAC
AGCAACTCCTCCAAGAGGGTATCTCATTAGGTAATTCAGAGGCAGACAGACAATTGCTGGAAGCTGCAA
AGGCTGGAGATGTGAACTGTAAAAAACTGTGTACTGTTTCAGAGTGTCAACTGCAGAGACATTGAAG
GGCGTCAGTCTACACCACTTCATTTTGCAGCTGGGTATAACAGAGTGTCCGTGGTGGAAATATCTGCTAC
AGCATGGAGCTGATGTGCATGCTAAAGATAAAGGAGGCCTTGACCTTTGCACAATGCATGTTCTTATG
GACATTATGAAGTTGCAGAACTTCTTGTTAAACATGGAGCAGTAGTTAATGTAGCTGATTTATGGAAAT
TTACACCTTTACATGAAGCAGCAGCAAAAGGAAAATATGAAATTTGCAAACTTCTGCTCCAGCATGGTG
CAGACCCTACCAAAAAAACAGGGATGGAAATACTCCTTTGGATCTTGTTAAAGATGGAGATACAGATA
TTCAAGATCTGCTTAGGGGAGATGCAGCTTTGCTAGATGCTGCCAAGAAGGGTTGTTTAGCCAGAGTGA
AGAAGTTGTCTCTCCTGATAATGTAAATTGCCGCGATACCCAAGGCAGACATTCAACACCTTTACATT
TAGCAGCTGGTTATAATAATTTAGAAGTTGCAGAGTATTTGTTACAACACGGAGCTGATGTGAATGCCC
AAGACAAAGGAGGACTTATTCCTTTACATAATGCAGCATCTTACGGGCATGTAGATGTAGCAGCTCTAC
TAATAAAGTATAATGCATGTGTCAATGCCACGGACAAATGGGCTTTACACCTTTGCACGAAGCAGCCC
AAAAGGGACGAACACAGCTTTGTGCTTTGTTGCTAGCCCATGGAGCTGACCCGACTCTTAAAAATCAGG
AAGGACAAACACCTTTAGATTTAGTTTCAGCGGATGATGTCAGCGCTCTTCTGACAGCAGCCATGCCCC
CATCTGCTCTGCCCTCTTGTTACAAGCCTCAAGTGCTCAATGGTGTGAGAAGCCCAGGAGCCACTGCAG
ATGCTCTCTCTTCAGGTCCATCTAGCCCATCAAGCCTTTCTGCAGCCAGCAGTCTTGACAACCTTATCTG
GGAGTTTTTTCAGAACTGTCTTCAGTAGTTAGTTCAAGTGGAACAGAGGGTGCTTCCAGTTTGGAGAAAA
AGGAGGTTCCAGGAGTAGATTTTAGCATAACTCAATTCGTAAGGAATCTTGGACTTGAGCACCTAATGG
ATATATTTGAGAGAGAACAGATCACTTTGGATGTATTAGTTGAGATGGGGCACAAGGAGCTGAAGGAGA
TTGGAATCAATGCTTATGGACATAGGCACAACTAATTAAAGGAGTCGAGAGACTTATCTCCGGACAAC
AAGGTCTTAACCCATATTTAACTTTGAACACCTCTGGTAGTGGAACAATTCTTATAGATCTGTCTCCTG
ATGATAAAGAGTTTCAGTCTGTGGAGGAAGAGATGCAAAGTACAGTTCGAGAGCACAGAGATGGAGGTC
ATGCAGGTGGAATCTTCAACAGATACAATATTCTCAAGATTGAGAAGGTTTGTAAACAAGAACTATGGG
AAAGATACACTCACCGGAGAAAAGAAGTTTCTGAAGAAAACCACAACCATGCCAATGAACGAATGCTAT
TTCATGGGTCTCCTTTTGTGAATGCAATTATCCACAAAGGCTTTGATGAAAGGCATGCGTACATAGGTG
GTATGTTTGGAGCTGGCATTATTTTGTGCTGAAAACCTTCCAAAAGCAATCAATATGTATATGGAATTG
GAGGAGGTACTGGGTGTCCAGTTCACAAAGACAGATCTTGTTACATTTGCCACAGGCAGCTGCTCTTTT
GCCGGGTAACCTTGGGAAAGTCTTTCCTGCAGTTTCAGTGCAATGAAAATGGCACATTCTCCTCCAGGTC
ATCACTCAGTCACTGGTAGGCCAGTGTAATGGCCTAGCATTAGCTGAATATGTTATTTACAGAGGAG
AACAGGCTTATCCTGAGTATTTAATTACTTACCAGATTATGAGGCCTGAAGGTATGGTCGATGGATAAA
TAGTTATTTTAAAGAACTAATTCCACTGAACCTAAAAATCATCAAAGCAGCAGTGGCCTCTACGTTTTAC
TCCTTTGCTGAAAAA

FIG._2B

SEQ ID NO: 3

Amino Acid Sequence Tankyrase Homologue isotype1

GFGRKDVVEYLLQNGASVQARDDGGLIPLHNACSFGEVNVNLLLRHGADPNARDNWNYPPLHEAAIKG
KIDVCIVLLQHGAEP TIRNTDGR TALDLADPSAKAVLTGEYKKDELLESARSGNEEKMMALLTPLNVNC
HASDGRKSTPLHLAAGYNRVKIVQLLLQHGADVHAKDKGDLVPLHNACSYGHEVTELLVKHGACVNAM
DLWQFTPLHEAASKNRVEVCSLLLSYGADPTLLNCHNKS AIDLAPTQLKERLAYEFKGHSLQAAEA
DVTRIKKHL SLEMVNF KHPQTHETALHCAA SPYPKRKQICELLRKGANINEKTKEFLTPLHVASEKA
HNDVVEVVVKHEAKVNALDNLGQTS LHRAAYCGHLQTCRLLLSYGCDPNIIISLQGF TALQMGNENVQQL
LQEGISLGNSEADRQLLEAAKAGDVETVKKLCTVQSVNCRDIEGRQSTPLHFAAGYNRVSVVEYLLQHG
ADVHAKDKGGLVPLHNACSYGHEVAELLVKHGAVNVADLWKFTPLHEAAAKGKYEICKLLLQHGADP
TKKNRDGNTPLDLVKDGD TDIQDLLRGDAALLDAAKKGCLARVKKLSSPDNVNCRDTQGRHSTPLHLAA
GYNNLEVAEYLLQHGADVNAQDKGGLIPLHNAASYGHVDVAALLIKYNACVNATDKWAFTPLHEAAQKG
RTQLCALLLAHGADPTLKNQEGQTPLDLVSADDVSALLTAAMPSPSALPSCYKPQVLNGVRS PGATADAL
SSGPSSPSSL SAASSLDNLSGSFSELSSVVSSSGTEGASSLEKKEVPGVDFSITQFVRNLGLEHLMDIF
EREQITLDVLVEMGHKELKEIGINAYGHRHKLIGVERLISGQQGLNPYLTLNTSGSGTILIDLSPDDK
EFQSVEEEMQSTVREHRDGGHAGGIFNRYN ILKIQKVCNKKLWERYTHRRKEVSEENHNHANERMLFHG
SPFVNAI IHKGFDERHAYIGGMFGAGIYFAENSSKSNQYVYGIGGGTGCPVHKDRSCYICHRQLLFCRV
TLGKSFLQFSAMKMAHSPPGHHSVTGRPSVNGLALAEYVIYRGEQAYPEYLITYQIMRPEGMVDG

FIG._3

SEQ ID NO: 4

Amino Acid Sequence Tankyrase Homologue isotype2

RCSARRGAAGGQGAQRGARVGAAHGTAPDPVTAGSQAARALSASSPGGLALLLAGPGLLLRLLALLLAV
AAARIMSGRRRCAGGGAACASAAAEAVEPAARELFEACRNGDVERVKRLVTPEKVNSRDTAGRKSTPLHF
AAGFGRKDVVEYLLQNGANVQARDDGGLIPLHNACSFHAEVNNLLLRHGADPNARDNWNYPPLHEAAI
KGKIDVCIVLLQHGAEP TIRNTDGRTALDLADPSAKAVLTGEYKKDELLESARSGNEEKMMALLTPLNV
NCHASDGRKSTPLHLAAGYNRVKIVQLLLQHGAADVHAKDKGDLVPLHNACSYGHEVTELLVKHGACVN
AMDWQFTPLHEAASKNRVEVCSLLLSYGADPTLLNCHNKS AIDLAPTQPKERLAYEFKGHSLQAAAR
EADVTRIKKHL SLEMVNFKHPQTHETALHCAAASPYPKRKQICELLRKGANINEKTKEFLTPLHVASE
KAHNDVVEVVVKHEAKVNALDNLGQTS LHRAAYCGHLQTCRLLLSYGCDPNIISLQGFTALQMGNEENVQ
QLLQEGISLGNSEADRQLLEAAKAGDVETVKKLCTVQSVNCRDIEGRQSTPLHFAAGYNRVSVVEYLLQ
HGADVHAKDKGGLVPLHNACSYGHEVAELLVKHGAVNVADLWKFTPLHEAAAKGKYEICKLLLQHGA
DPTKKNRDGNTPLDLVKDGD TDIQDLLRGDAALLDAAKKGCLARVKKLSSPDNVNCRDTQGRHSTPLHL
AAGYNNLEVAEYLLQHGAADVNAQDKGGLIPLHNAASYGHVDVAALLIKYNACVNATDKWAFTPLHEAAQ
KGRTQLCALLLAHGADPTLKNQEGQTPLDLVSADDVSALLTAAMPPSALPSCYKPQVLNGVRS PGATAD
ALSSGPSSPSSLSAASSLDNLSGSFSELSSVVSSSGTEGASSLEKKEVPGVDFSITQFVRNLGLEHLMD
IFEREQITLDVLVEMGHKELKEIGINAYGHRHKLIGKVERLISGQQLNPYLTNTSGSGTILIDLSPD
DKEFQSVEEEMQSTVREHRDGGHAGGIFNRYNLIKIQKVCNKKLWERYTHRRKEVSEENHNHANERMLF
HGSPFVNAI IHKGFDERHAYIGMFGAGIYFAENSSKSNQYVYGIGGGTGCPVHKDRSCYICHRQLLFC
RVTLGKSFLQFSAMKMAHSPPGHHSVTGRPSVNGLALAEYVIYRGEQAYPEYLITYQIMRPEGMVDG

FIG._4

Schematic Presentation of Dominant Negative Mutants for Tankyrase Homologue

Dominant Negative Mutants

Truncation: 429 Δ C- of the C-terminal catalytic domain – truncation of the catalytic domain of PARP acts as a dominant negative when overexpressed *in vivo* (Oncogene 1999 Nov 25; 18(50):7010-5)

Point mutant: E945A Δ C- conserved residue in PARP domain, thought to be important in NAD⁺ binding

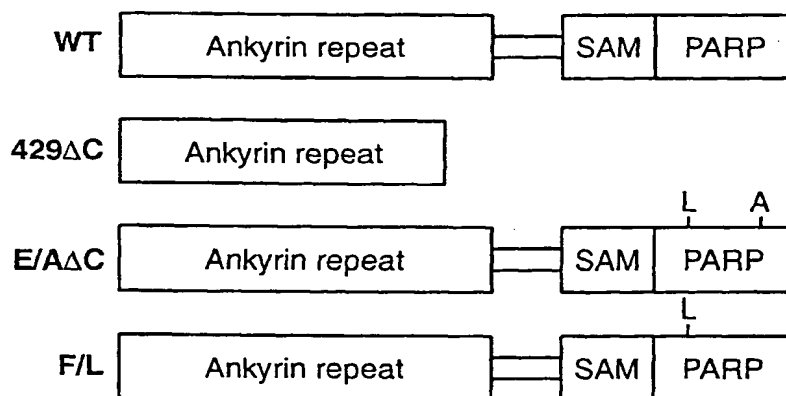


FIG. 5

**Cell Cycle Analysis of A549 Cells
Infected With GFP-fused Wild Type
and Mutant Tankyrase Homologue**

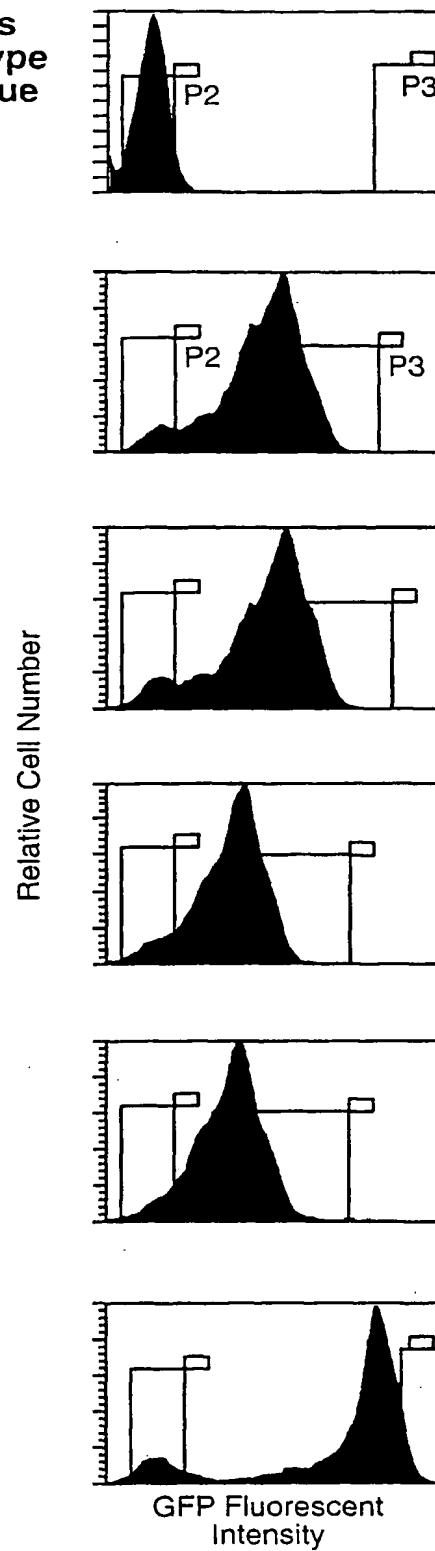


FIG._6A

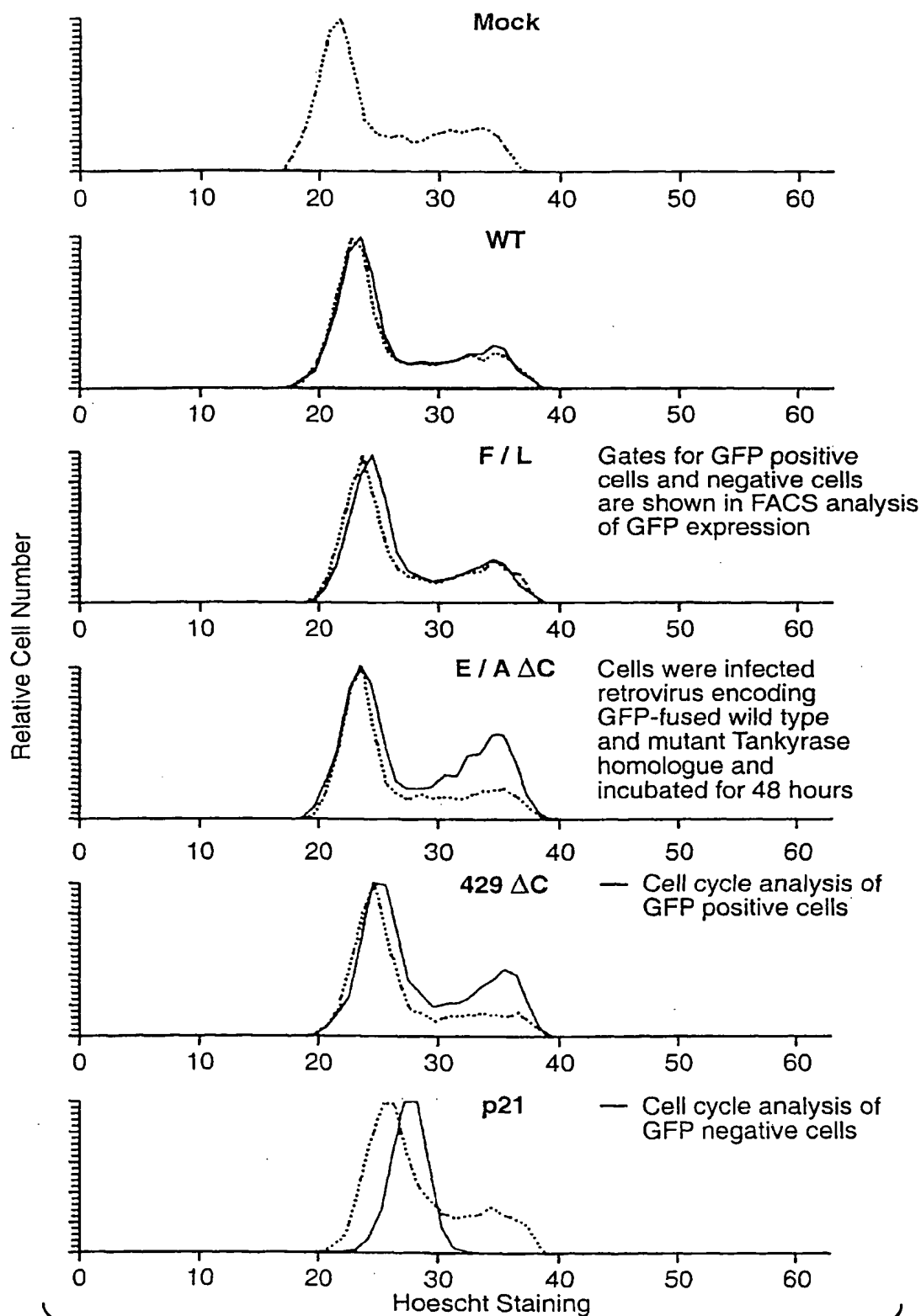


FIG._6B

Kinetics of GFP Positive cells in A549 Cells and Human Mammary Epithelial Cells (HMEC) After Retrovirus Infection Encoding GFP-fused Wild Type and Mutant Tankyrase Homologue

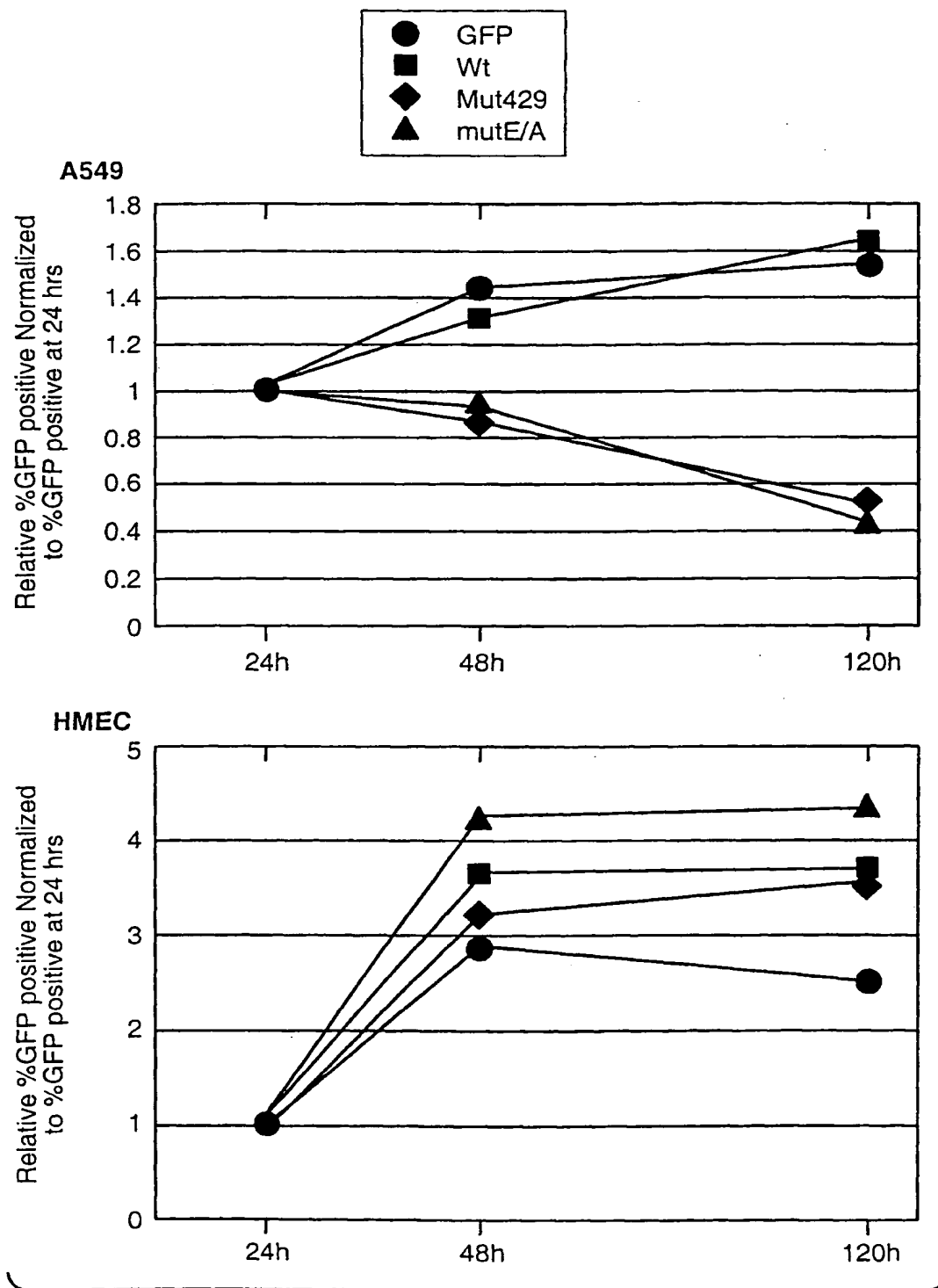
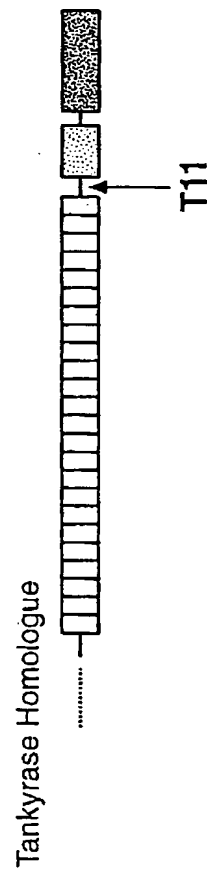


FIG._7

The Binding Site of Antisense Oligos Against Tankyrase Homologue



□ Ankyrin repeat ■ SAM ▨ PARP



..... Unidentified sequence

T11

	GTGGAACACAGAGGGTGCTTCC	
Tankyrase Homologue	GTGGAACACAGAGGGTGCTTCCAGTTTGAGAAAAAGGAGGTTCCAGAGTAGATTTAGCAT	2838
Tankyrase	ATGCAGGGGATGGCGCCCGCGGGAACAGAAAAAGGAAGGAGAGAAAGTTGCTGGTCTTGACAT	3091
	** * ** * * * * * * * * * * * * * * * * * * * *	

FIG._8

Anti-Proliferative Phenotype of Antisense Oligonucleotides Against Tankyrase Homologue in A549 and HeLa Cells

 T11-SCR
 T11

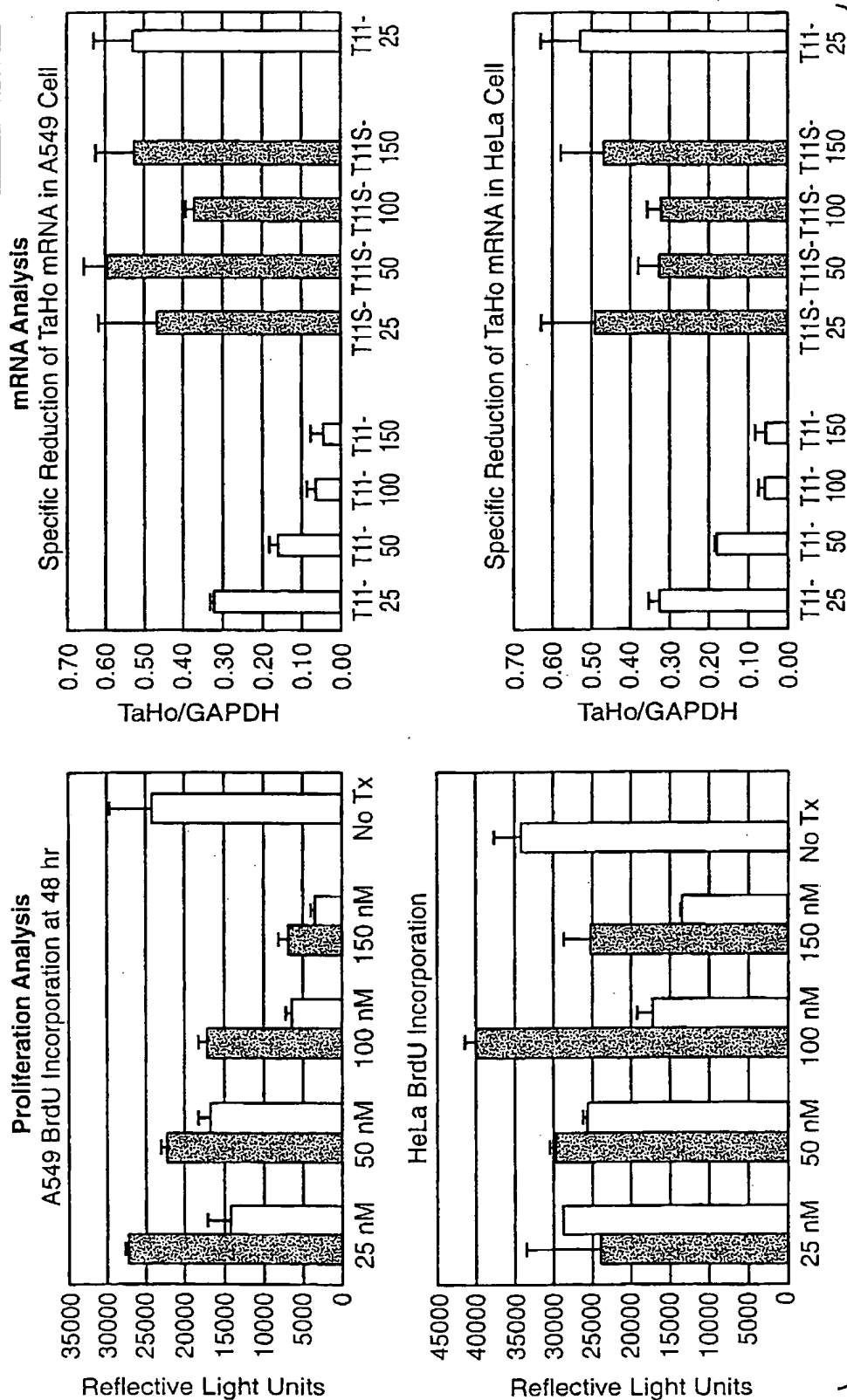


FIG._9

Cell Cycle Analysis of A549 Cells Transfected with Antisense Oligonucleotides Against Tankyrase Homologue at 48 Hours, Antisense Oligonucleotides (T11) and Control Oligonucleotides (T11S) were transfected with FITC-labeled random 20mer Oligonucleotides (FITC), After 48 Hours, entire population (R1) and Top 5% (R2) of FITC transfected cells were analyzed for cell cycle

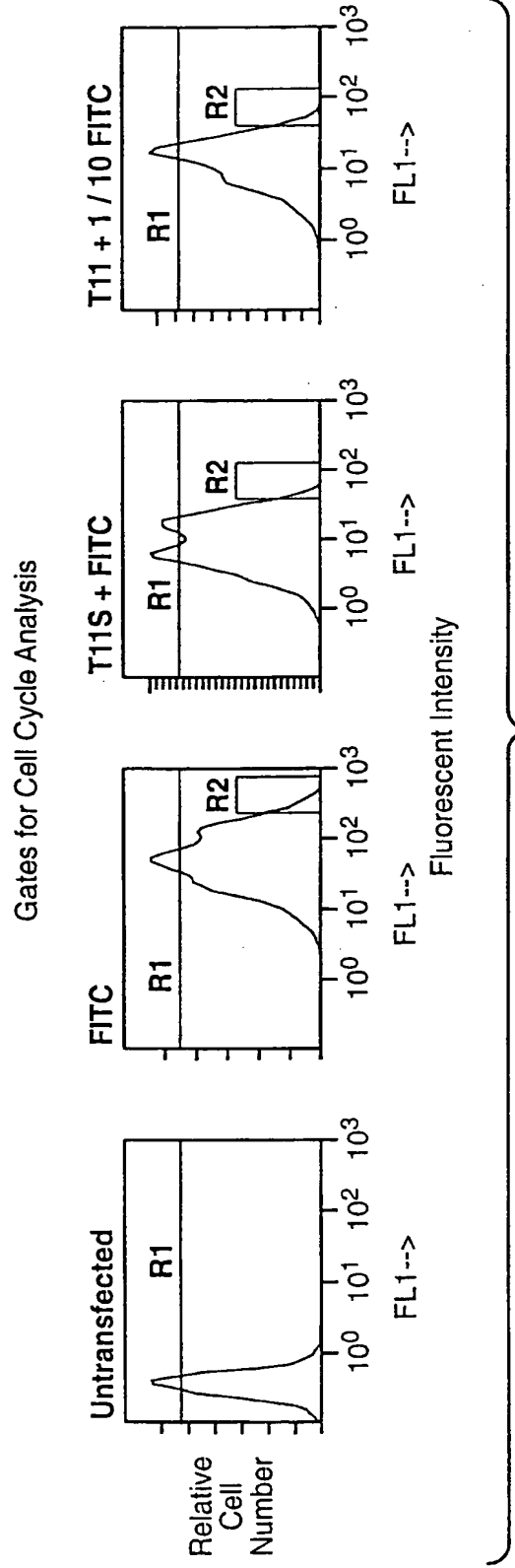


FIG. 10A

Cell Cycle Analysis of A549 Cells Transfected with Antisense Oligonucleotides Against Tankyrase Homologue at 48 Hours, Antisense Oligonucleotides (T11) and Control Oligonucleotides (T11S) were transfected with FITC-labeled random 20mer Oligonucleotides (FITC). After 48 Hours, entire population (R1) and Top 5% (R2) of FITC transfected cells were analyzed for cell cycle

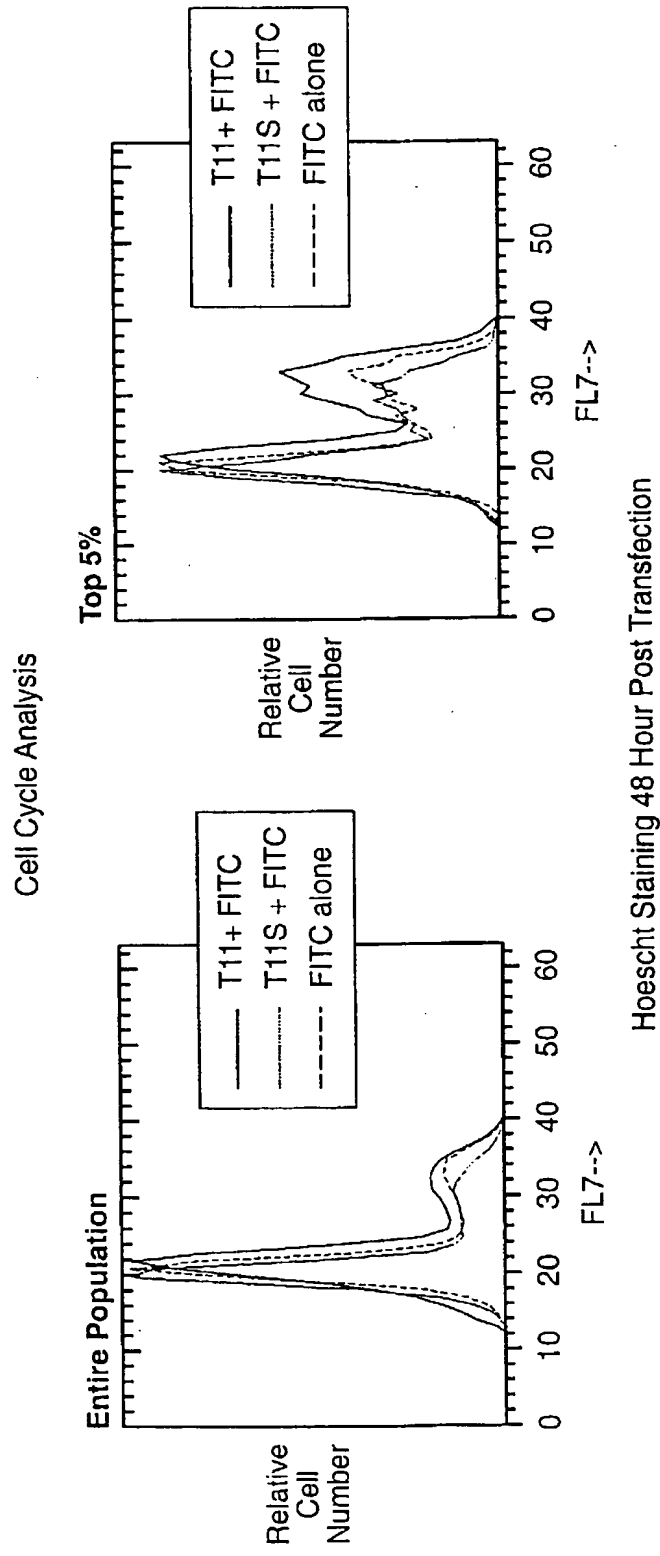


FIG. 10B

mRNA Expression of Tankyrase Homologue in Several Tumors and Normal Tissues by a Taqman Analysis, mRNA Expression was Normalized by 90kDa Highly Basic Protein (HBP) and Ribosomal Protein S9 (S9)

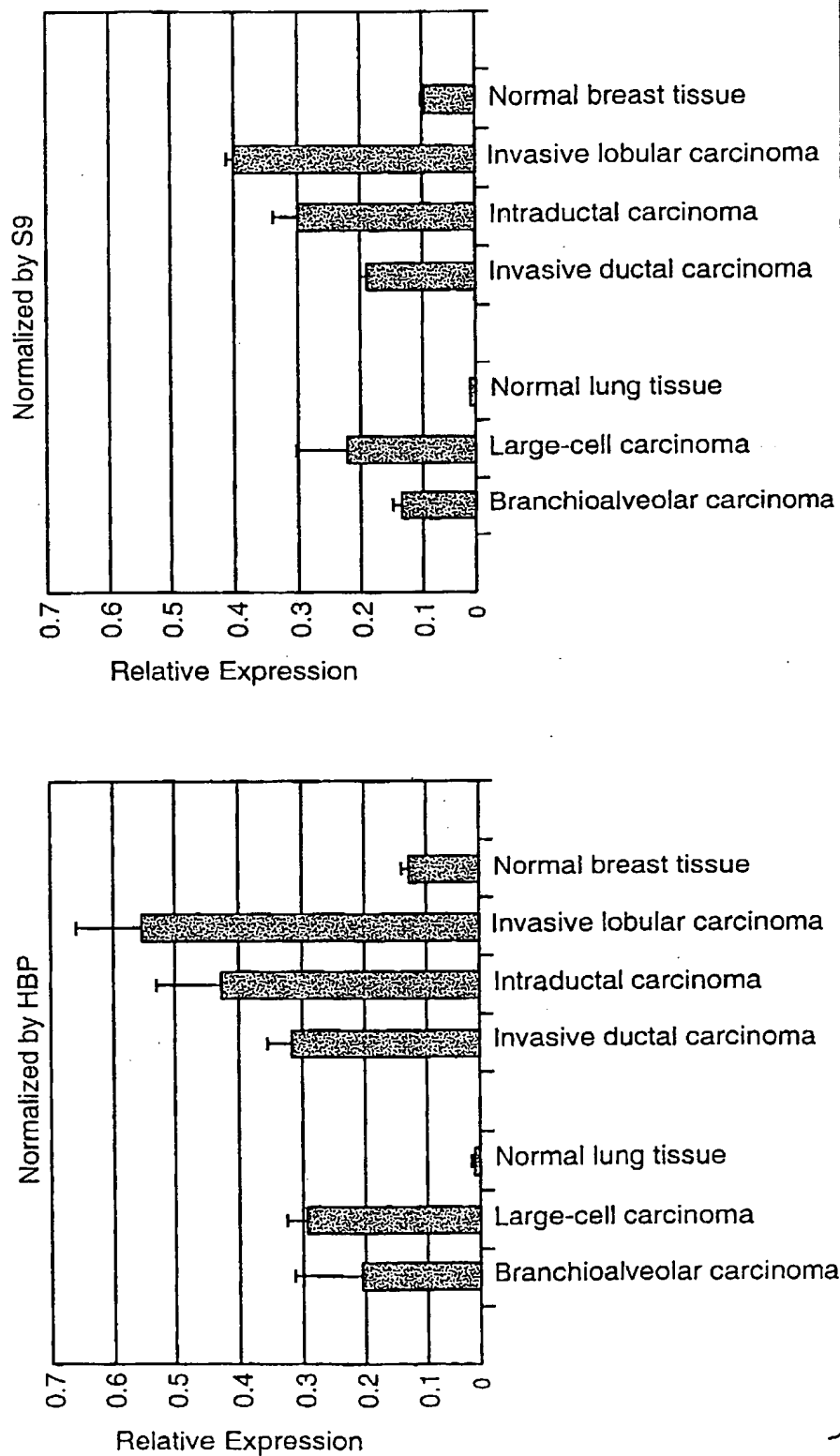


FIG. 11

**Procedure for Nonisotopic Detection of Poly-ADP Ribosylation
Using Anti-GFP mAb-Coated Plates**

Protein lysates from 293T cells normalized by GFP
fluorescence and total protein

↓
Immobilization of GFP-tankyrase homologue in anti-
GFP Coated plates

↓
Auto PARP reaction with Biotinylated-NAD in 96 wells

↓
Detection of poly ADP ribose chains with Streptavidin-
HRP and chemiluminescent substrate

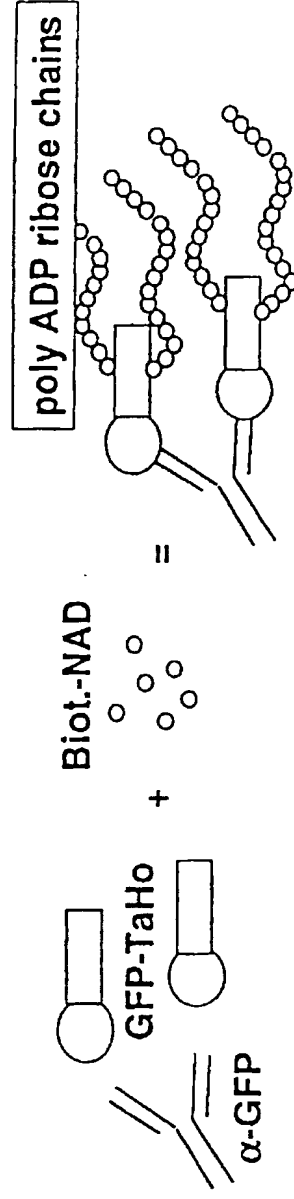


FIG._12

Non-Isotopic Plate-Based Detection of TaHo PARP Activity in the Presence of Biotinylated NAD

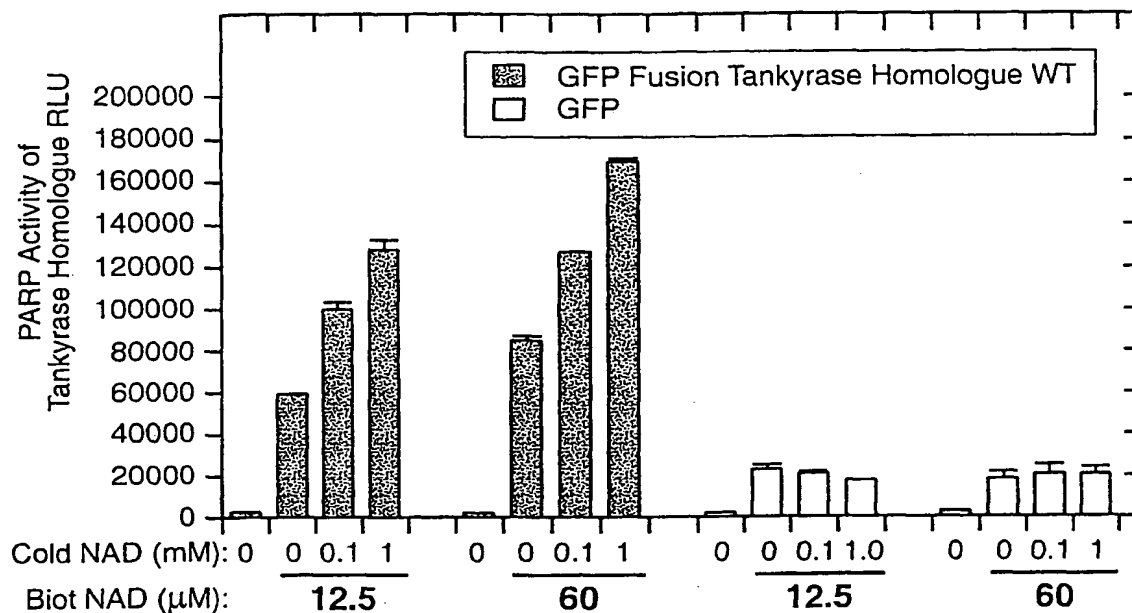


FIG. 13

Comparison of IC₅₀ Values of the PARP Inhibitors

	Approximate IC ₅₀ (nM)	hPARP assay IC ₅₀ (nM)		
	TaHo	Rigel	Decker*	Rankin*
3AB	>50 000	5 000	2 000	5 400
6(5H)Phenanthridinone	1 000-2 000	300		
Niacinamide	>50 000	30 000	>>5 000	31 000

* Decker P et al., Clinical Cancer Research. 1999 May; 5:1169-1172

* Rawkin PW et al., J Biol Chem. 1989 Mar 15;264(8):4312-4317

FIG. 14

**Inhibition of Tankyrase Homologue PARP Activity
by hPARP Inhibitors**

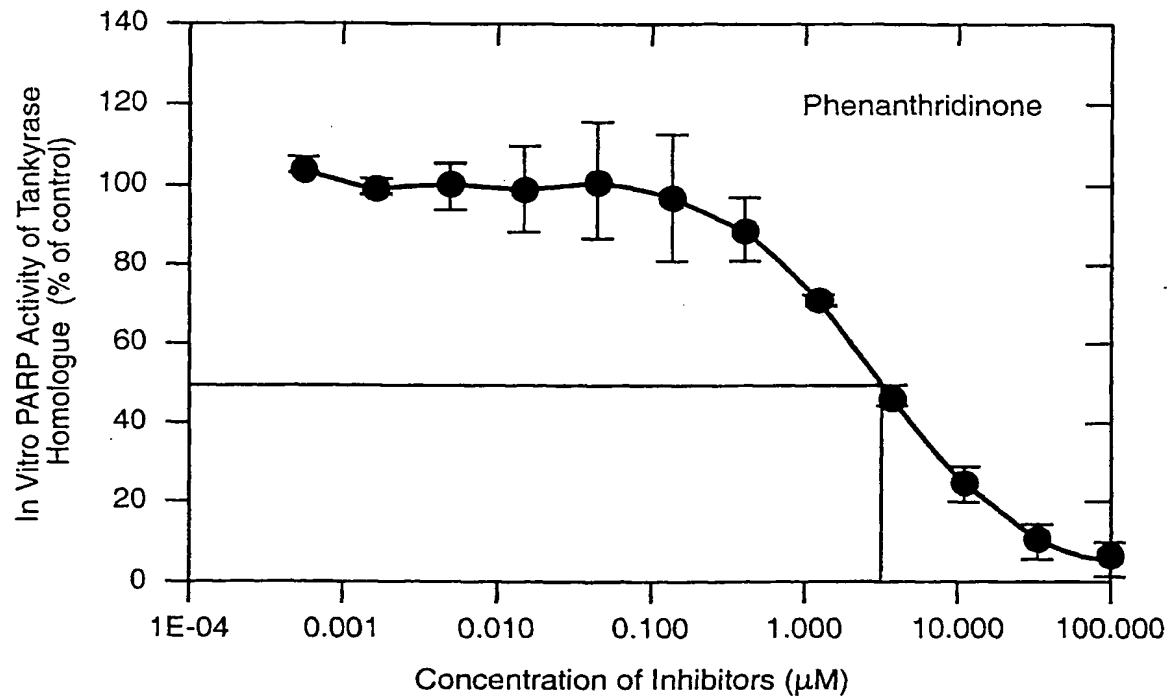


FIG._15

TH-1: Tankyrase Homologue isoform-1, TH-2: Tankyrase Homologue isoform-2 FIG. 16A
M (Red): the first methionine in the sequence, Z: stop codon
In this figure, the first methionine in TH-1 sequence is position 1 (M1)

Taho C terminus deletion mutant ends at position 429 (K) and adds 28 amino acids because of frame shift.

Taho F/L mutant has the mutation at position 871

Taho E/A dC mutant has the mutation at position 948, ends at position 957 (A) and adds 2 amino acids.

TH-1	-----	
TH-2	RCSARRGAAGGQGAQRGARVGAAHGTAPDPVTAGSQ	-231
TH-1	-----	
TH-2	AARALSASSPGGLALLAGPGLLLRLLALLAVAAARIMSGRRRCAGGGAACASAAAEAVE	-171
TH-1	-----	
TH-2	PAARELFEACRNGDVERVKRLVTPEKVNSRDTAGRKSTPLHFAAGFGRKDVVEYLLQNGA	-111
	Ankyrin repeat	Ankyrin repeat
TH-1	SVQARDDGGLIPLHNACSFGEVNVNLLLRHGADPNARDNWNYPPLHEAAIKGKIDVCIV	-51
TH-2	NVQARDDGGLIPLHNACSFGEVNVNLLLRHGADPNARDNWNYPPLHEAAIKGKIDVCIV	-51
	Ankyrin repeat	Ankyrin repeat
		•TH1 start
TH-1	LLQHGAETIRNTDGR TALDADPSAKAVLTGEYKKDELLESARSGNEEKMALLTPLNV	10
TH-2	LLQHGAETIRNTDGR TALDADPSAKAVLTGEYKKDELLESARSGNEEKMALLTPLNV	10

FIG._16B

TH-1	_____	Ankyrin repeat	_____	Ankyrin repeat
TH-2	NCHASDGRKSTPLHLAAGYNRVKIVQLLLQHGADVHAKDKGDLVPLHNACSYGHYEVTEL 70			
	NCHASDGRKSTPLHLAAGYNRVKIVQLLLQHGADVHAKDKGDLVPLHNACSYGHYEVTEL 70			
	_____	Ankyrin repeat	_____	Ankyrin repeat
TH-1	LVKHGACVNAMDLWQFTPLHEAASKNRVECSLLLSYGADPTLLNCHNKSAIDLAPTQL 130			
TH-2	LV			
	_____	Ankyrin repeat	_____	
TH-1	KERLAYEFKGHSLLOAAREADVTRIKKHLSEMNVNFKHPQTHETALHCAAASPYPKRKQI 190			
	_____	Ankyrin repeat	_____	Ankyrin repeat
TH-1	CELLLRKGANINEKTKEFLTPLHVASEKAHNDVVEVVVKHEAKVNALDNLGQTSLHRAAY 250			
	_____	Ankyrin repeat	_____	
TH-1	CGHLQTCRLLLSYGCDPNIISLQGFALQMGNEVQQLLQEGISLGNSEADRQLLEAKA 310			
	_____	Ankyrin repeat	_____	Ankyrin repeat
TH-1	GDVETVKKLCTVQSVNCRDIEGRQSTPLHFAAGYNRVSVVEYLLQHGADVHAKDKGGLVP 370			
	_____	Ankyrin repeat	_____	Ankyrin repeat
TH-1	LHNACSYGHYEVAE ^T LLVKHGAVNVVADLWKFTPLHEAAAKGKYEICKLLLLQHGADPTKKN 430			
	_____	Ankyrin repeat	_____	Ankyrin repeat
				Deletion---
TH-1	GMEILLWILLKMEIQIFKICLGEMQLCZ			
	RDGNTPLDLVKDGTDIQDLLRGDAALLDAAKKGCLARVKKLSSPDNVNCRDTQGRHSTP 490			
	_____	Ankyrin repeat	_____	

FIG. 16C

TH-1	LHLAAGYNNLEVAEYLLQHGADVNAQDKGLIPLHNAASYGHVDVAALLIKYNACVNATD 550 Ankyrin repeat Ankyrin repeat
TH-1	KWAFPLHEAAQKRTQLCALLLAHGADPTLKNQEGQTPLDLSADDDVSALLTAAMPSPA 610 Ankyrin repeat Ankyrin repeat
TH-1	LPSCYKPPQVLNGVRSPGATADALSSGPPSPSSLSAASSLDNLGSGFSELSSVVSSGTEG 670 Ankyrin repeat
TH-1	ASSLEKKE--VPGVDFSITQFVRNLGLEHLMDFIEREQITLDVLVEMGHKELKEIGINAY 730 SAM domain
TH-1	GHRHKLIKVERLISQQQGLNPYLTNTSGSGTILIDLSPDDKEFQSVEEEMQSTVREHR 790
TH-1	DGGHAGGIFNRYNLIKQVCNKKLWERYTHRRKEVSEENHNHANERMLFHGSPFVNAIL 850
TH-1	HKGFDERHAYIGGMFGAGIYFAENSSKSNQYVYGIGGTGCPVHKDRSCYICHRQLLFCR 910 • F→L mutation PARP domain
TH-1	VTLGKSFLQFSAMKMAHSPPGHHSVTGRPSVNGLALAEYVIYRGEQAYPEYLITYQIMRP 970 •E→A •Deletion. -----A-----LSZ
TH-1	EGMVDG 976